Automated Analyses of Behavior in Zebrafish Larvae

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Early brain development may be influenced by numerous genetic and environmental factors with long-lasting effects on brain function and behavior. Identification of these factors is facilitated by behavioral studies in animal model systems. However, large-scale screening in whole organisms remains challenging. We developed a novel high-throughput imaging system capable of analyzing complex behaviors in zebrafish larvae. The three-camera system can image twelve multi-well plates simultaneously and is unique in its ability to provide local visual stimuli in the wells of a multi-well plate. The acquired images are converted into a series of coordinates, which characterize the location and orientation of the larvae. The imaging techniques were tested by measuring avoidance behaviors of zebrafish larvae in response to visual stimuli. The system effectively quantified larval avoidance responses and revealed an increased edge preference in response to a 'bouncing ball' stimulus. We further demonstrated that this edge preference, or thigmotaxis, can be interpreted as a measure of anxiety; larvae exposed to valium showed a reduced edge preference, while larvae exposed to caffeine showed an increased edge preference. We are currently using the developed imaging system to screen for behavioral defects in response to modulators of calcium signaling and organophosphate pesticides. The imaging system and assays for measuring avoidance behavior may also be used to screen for a variety of other genetic and environmental factors that cause developmental brain disorders and for novel drugs that could prevent or treat these disorders.